THE PERIPHERAL BLOOD CIRCULATION AND THE [illegible]
OF THE VESSEL WALLS IN THE DYNAMICS OF [illegible]

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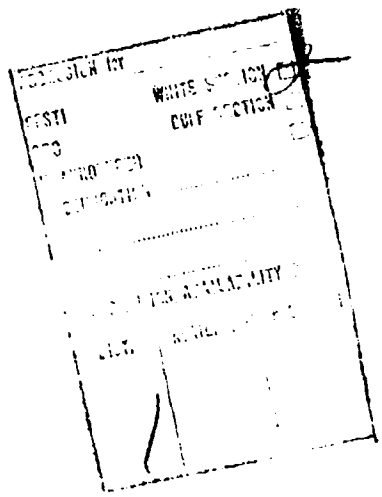

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THE PERIPHERAL BLOOD CIRCULATION AND THE PERMEABILITY OF THE VESSEL WALLS IN THE DYNAMICS OF EXPERIMENTAL PLAGUE

[Following is the translation of an article by K. M. Mokhin, published in the Russian-language periodical Trudy Rostovskogo-na-Donu Gosudarstvennogo Nauchno-Issledovatelskogo Protivochumnogo Instituta (Trudy of the Rostov/Don State Scientific-Research Antiplague Institute), Vol XV, installment 1, 1959, pages 71--85. Translation performed by Sp/7 Charles T. Ostertag, Jr.]

The end goal of the function of blood circulation is realized in the capillary system -- the transfer to the working cells of the nutrient substances which are necessary for their activity and the outlet of products of tissue metabolism. Therefore, in the end result the condition of the working tissues and organs may depend on the condition of capillary circulation.

It is known that the intensity of capillary blood flow changes not only during pathological conditions, but also is subject to fluctuations following a change in the functional condition of the organism. If during the relative quiet of the organ or tissue part of the capillaries are found in a sleeping condition, then in the functioning tissue the opening of additional capillaries takes place, the capacity of the capillary net is significantly increased and the rate of blood flow increases. The increase in the number of functioning capillaries and the accelerated blood flow in them guarantee the increasing needs of the tissues and organs in oxygen, nutrient substances, and the removal of the products of metabolism.

Normal collateral mechanisms may be insufficient or lacking during pathological conditions of the organism, and this leads to a worsening of the tissue blood circulation in the viably important organs and systems and a disruption of their functional performance.

Under the conditions of a normal functioning organism the intensity of metabolism between the blood and tissues is determined primarily by the rate of the capillary blood flow and the number of functioning capillaries (I. I. Islamov, 1954; B. D. Zabudskiy, 195[illegible]; Kety, 1949; Schmucking, 1951; Rpaport, Saul, Hyman, Morton, 1952; Coste, Bourel, Morel, 1954; and others).

During pathological conditions the amount of nutrient substances and oxygen reaching the tissues and also the metabolic products removed from the tissues will depend, in addition to the magnitude of the resorption

surface of the capillaries and the rate of blood circulation in them, on the state of permeability of the vascular endothelium. With other conditions being equal, it is understandable that with a disruption of the permeability of the vascular wall there is a change in the amount and the rate of substances passing from the blood into the tissues and from the tissues into the blood.

Up until recently objective investigations of the dynamics of metabolic processes between the tissues and the blood have met with methodical difficulty. With the application of labeled atoms in medicine, new, more thorough methods were found for studying capillary blood circulation. Here the principle of investigating the tissue blood flow amounts to the intracutaneous, subcutaneous or intramuscular administration of indicator substances of an artificial isotope and the determination of the rate of its removal beyond the site of administration. By recording the activity of radiation above the site of administration over short periods of time, it is possible to make conclusions concerning the intensity of removal of the radioactive substance.

The first time following the administration of the isotope into a tissue the rate of its resorption decreases evenly. Subsequently, by the end of the determination, the intensity of radiation is reduced less, which is connected with the fixation of the radioactive substance by the tissues at the site of administration (Islamov, I. I., 1954; Helde, Seeberg, 1953). Therefore, it is considered that only in the first period following the injection of the isotope the decrease in the activity of radiation reflects the rate of resorption. In view of this it is usual to record, not the time over which the administered radioactive substance is completely removed beyond the site of injection, but the time during which the intensity of radiation is decreased by half (half removal).

It has been established that low molecular compounds are removed from the tissues by means of their resorption by the blood carrying capillaries, whereas high molecular compounds are removed beyond the site of administration by the system of lymph capillaries (I. I. Islamov, 1954; Kety, 1949; Jepson, Simeone, Dobyns, 1953; Rowson, Morgon, 1954). Thus, the rate of removal from the tissues of the isotopes which are included in the composition of low molecular inorganic compounds may characterize the condition of the capillary blood circulation, and based on the intensity of resorption of high molecular substances (usually labeled albumin or globulin) produce a conclusion concerning the peculiarities of lymph circulation.

The objective and accurate method of using artificial radioactive isotopes for studying the condition of tissue blood circulation during various physiological and pathological conditions of the organism has come into extensive practice both experimentally as well as in clinical investigations.

In studying the condition of the cardiovascular system during plague infection, we decided to include in the circle of our investigations a

determination, utilizing the method of labeled atoms, of the peculiarities of capillary blood circulation in various periods following the infection of animals with B. pestis.

The investigation of the capillary blood flow during experimental plague made it necessary to study not only the capillary system as part of the cardiovascular system, but also the dictatively seperately expressed degree of permeability of minute vessels and capillaries during plague.

The data of pathologoanatomical and histological investigations point to the significant changes in the capillaries during all forms of plague. In previous communications we pointed out that already Albrecht and Ghon (1898, 1900) noted the significant affection of the capillaries of the parenchymatous organs. D. P. Kishenskiy et al. (1911) wrote about the deep changes in the blood vessels, including the capillaries. In cases of experimental plague infection in guinea pigs, expressed changes in the capillary structures in the organs of the reticuloendothelial system were observed by V. V. Donskov (1944).

On the basis of an analysis of literary sources and rich local materials, V. N. Lobanov (1956) came to a conclusion concerning the affection of minute vessels and capillaries in all the tissues and organs, both during experimental plague as well as during plague in man. In view of the fact that the severity of affections of the vascular system usually were more significant than changes in the cardiac muscle, V. N. Lobanov made a proposal concerning the leading role of vascular affliction in disorders of hemodynamics, and expressed the necessity of reviewing the problem concerning the causes of death of an organism during plague.

At the same time that the morphological changes in the capillaries during plague were noticed many times by many authors, the nature and degree of functional disruptions in the capillary system during this infection have not been studied at all.

The present article presents the results of an experimental study made by us of the functional condition of the capillaries during plague in guinea pigs.

Methods

The tests were set up on guinea pigs weighing 400--470 grams. In the sheared area of the animal we used a tuberculin syringe to administer subcutaneously an 0.1 ml dose of a solution of P^{32} in the form of dibasic sodium phosphate. The concentration of P^{32} was selected in such a way that in the beginning of the recording the number of impulses in 1 minute would be within the limits of 1,000.

The recording of impulses was performed with a "B" apparatus with an AS-2 calculator embedded in a lead film with an aperture 12 mm in diameter.

The calculator was situated 1 cm over the site of administration of the radioactive substance. During the test the recording of the intensity of radiation lasted one minute with one minute breaks.

The intensity of resorption of the administered isotope was determined 3--4 times on healthy guinea pigs, after which they were infected subcutaneously with the B. pestis 773 virulent strain (infecting dose -- 1,000 microbial bodies which comprised 100 Dlm). Subsequently the condition of the capillary blood flow was determined in the dynamics of plague infection.

At the same time the pathologoanatomical and bacteriological picture of the infectious process were investigated. For this, daily following the determination of the rate of resorption of the administered isotope, we dissected 1--2 guinea pigs, determined the nature and degree of the pathologoanatomical changes and made seedings on agar media from the subcutaneous cellular tissue at the site of injection of B. pestis, the regional lymph node, spleen, liver, lungs, and blood.

Results of the tests and a discussion of them

For a judgement of the degree of disruptions of the functional condition of the capillaries during experimental plague infection, it was necessary first of all to establish the limits of the physiological deviations in the rate of resorption of the subcutaneously administered $Na_2HP^{32}O_4$ in healthy guinea pigs. For this purpose the rate of resorption was determined 3--4 times for each guinea pig before infection.

For an explanation of the course of the investigation we will present the proceedings of one of the tests.

29 January 1957, guinea pig No. 8, weight 380 grams. Temperature of the premises 21°C. Initial background -- 72 impulses in 1 minute.

The guinea pig was fixed in the stand with the stomach up. Into the sheared area of the animal we administered subcutaneously 0.1 ml of physiological solution which had an additive of the indicator amount of $Na_2HP^{32}O_4$. For removing possible traces of radioactive phosphorus on the surface, the skin was rubbed with a moist cotton tampon. The AS-2 counter was secured at a distance of 1 cm over the site of administration. The intensity of radiation was recorded for one minute with one minute breaks. The data obtained is presented in table 1.

For calculating the time of half removal, the resulting values are conveniently expressed graphically. The graph is constructed in the system of semi-logarithmic coordinates. The time in minutes which passed from the onset of administration of the isotope is plotted on the axis of abscissae and the logarithm of the number of impulses is plotted on the axis of ordinates. Through the points which are plotted in this manner it is possible to draw a straight line, the slant of which depends on the rate of

resorption. A determination of the time for the half removal of the administered isotope according to the graph leads to the finding of the time for the decrease in the number of impulses by 2 times, which corresponds to a reduction of the lg of the number of impulses by 0.3. Use of the graph yields more accurate results than simple calculation, since it makes it easier to see possible accidental errors, which are not laid out in the graph.

A graphic representation of the data presented in table 1 is presented in figure 1, line N.

From figure 1 it is seen that the time for the half removal of the subcutaneously administered radioactive phosphorus P^{32} in healthy guinea pigs in the stated test equals 12 minutes.

The determination of the time of the half removal of the isotope in healthy guinea pigs showed that in them there are individual deviations in the intensity of resorption, since in the same animal the time for half removal (that is, the rate of resorption) over a period of 4--6 days changes little (table 2).

During the determination of the rate of resorption in infected guinea pigs it was established that already after one day of experimental plague infection, there is noted a reduction in the intensity of absorption of subcutaneously administered radioactive phosphorus. Thus, from table 3 and figure 1 (line 1), which represent the rate of resorption of radioactive phosphorus in guinea pig No. 8 after one day following infection, it is seen that the time of half removal equals 21.5 minutes.

The intensity of absorption of the subcutaneously administered radioactive phosphorus in this same guinea pig prior to infection is presented in table 1 and figure 1 (line N). A comparison shows that the time of half removal after a day following infection of the guinea pig with B. pestis increases by almost 2 times.

From an analysis of the results of the tests it follows that in the other animals already after 24 hours following infection the rate of absorption of $Na_2HP^{32}O_4$ is significantly decreased (table 4).

Thus, it is seen from table 4 that after 3 days following infection the time for the half removal of the subcutaneously administered radioactive phosphorus in guinea pig No. 8 increased up to 37 minutes. On the 4th day the time of half removal increased still more (49 minutes), and on the 5th day of plague infection exceeded the initial by more than 5 times (67 minutes).

A reduction in the rate of resorption of the subcutaneously administered isotope, progressing with the course of plague infection, was noted regularly in all cases of experimental infection of guinea pigs with B. pestis.

Statistical processing of the results show them to be fully reliable. In call cases $P < 0.001$.

We pointed out above that the rate of removal of the low molecular substances from the tissues depends on the functional condition of the capillaries and primarily on the rate of blood flow and permeability of the capillary wall. Therefore the slowing down of absorption of radioactive phosphorus from the subcutaneous cellular tissue of plague infected guinea pigs may be appraised as the result of a significantly expressed decrease in the rate of capillary blood circulation and a disruption of the permeability of the vascular wall.

It was shown by the investigators Kety (1949), Jacox, Johnson, Koontz (1952), I. I. Islamova (1954), and others that the rate of resorption of low molecular substances from the tissues depends primarily on the condition of the capillary blood circulation, and is determined to a lesser degree by the condition of permeability of the capillary wall. From this it should be possible to consider that the slowing down of absorption of radioactive phosphorus from the subcutaneous cellular tissues in guinea pigs infected with B. pestis causes primarily a disruption in the rate of the blood flow. However, we did not consider it possible to make a similar conclusion for the tissues of a plague animal without the appropriate experimental verification, and therefore, following the determination of the rate of absorption of radioactive phosphorus we decided to study also the rate of blood flow in guinea pigs during various phases of plague infection. With this aim we determined the rate of blood flow in 20 guinea pigs before infection and on each day following their infection with B. pestis (infecting dose -- 1,000 microbial bodies, which corresponds to 100 Dlm).

The determination of the rate of blood flow was performed with the help of cytisine solution.

It is known that cytisine solution, just as with lobeline, is a pharmacological preparation which excites the respiratory center. Following its intravenous administration a reflex excitability of the respiratory center sets in, and this leads to the emergence of profound respiratory movements. This property of cytisine solution and lobeline is used for determining the rate of blood flow in clinical and experimental investigations. For this the cytisine solution is introduced intravenously and the time is noted for the appearance of the first profound inspiration.

In our tests we made a small incision on the guinea pigs on the skin of the rear paw over the surface of a vein, and into this vein we introduced the standard dose of a solution of cytisine (0.05--0.1 ml). The changes in respiration were transmitted by a pneumatic system to a Maria capsule. The respiratory movements and time indications were recorded on kymograph tape.

The results of the study of the rate of blood flow in healthy guinea pigs and following their infection with B. pestis are presented in table 5.

It is seen from table 5 that the rate of the blood flow is slowed down as a measure of the development of the plague process and on the 5th day following infection, before the death of the animals, exceeds the initial one by 2 times.

By comparing the rate of resorption of radioactive phosphorus from the tissues to the blood (table 4) with the rate of flowing of the blood in plague infected animals (table 5), it can be noted that the rate of resorption of the isotope slows down more significantly than the blood flow is slowed down. These differences set in especially graphically, beginning with the 3--4th day of plague infection, when the rate of blood flow is slowed down on an average of 2 times, and the intensity of absorption of radioactive phosphores -- by 3.5--4 times.

Consequently, the slowing down of the processes of resorption of substances from the tissues to the blood during experimental plague in guinea pigs should be connected not with just the lowering of the rate of blood flow.

It is known that during infectious diseases an increase in the permeability of the capillary endothelium is observed. Thus, B. N. Mogilnitskiy and M. S. Brumshteyn (1949) noted a significant increase of vascular permeability during dysentery, Kh. L. Tregubova (1949) -- during diphtheria, measles and influenza; I. S. Novitskiy (1949) -- during brucellosis, B. N. Mogilnitskiy (1956) during diphtheria, S. A. Gornak (1956) -- during sepsis, etc.

In spite of the fact that during plague special determinations of vascular permeability were not conducted, all the same it is possible to presume the presence of increased permeability of the capillary wall also during this infectious disease. Already the presence of significant hemorrhages in plague speak for the increased permeability.

At first glance, it may appear that with the increased permeability of the vascular wall, nutrient substances and gases (oxygen, carbon dioxide) will pass through it easier than through intact vascular epithelium. Also in such a case the exit of products of tissue metabolism would be significantly eased, and the fact of the increase in permeability of the vascular membranes would be unconditionally a favorable moment. B. N. Mogilnitskiy et al. (1949--1956) showed that an increase of vascular permeability is accompanied by the outflow of plasma protein from the blood channel into the tissue. Along with this there takes place a saturation of the tissues and a blockade of the cellular elements set in with the subsequent disruption of nourishment, respiration, and the removal of products of cellular metabolism. Besides this, in cases of infectious diseases, bacterial poisons which cause the phenomenon of intoxication penetrate through the affected capillaries into the tissues.

Consequently, the disruption of the capillary endothelium, which is accompanied by an increase of its permeability, leads to plasmorrhea [?] and

the blockading of cellular elements by the protein masses which are coming out of the blood channel, which sharply disrupts the metabolism between the blood and the tissues. The discharge of plasma into the intertissue spaces causes the clotting of blood, a reduction of its volume, and the subsequent disruption of blood circulation. In this manner, it can be considered that the disruption of vascular permeability is a real factor in the genesis of many pathological processes.

In determining the content of oxygen in the blood during experimental plague of guinea pigs in a previous work, we noted that oxygen is no lower than 7.3 per cent by volume (on the average), though at this time there are all the signs of a more profound oxygen deficiency (shortness of breath, change of the T-wave on the electrocardiogram, decrease of glycogen in the myocardium). The assumption was expressed concerning the disruption of the transfer of oxygen through the capillary endothelium as a result of its affection. In the light of the data presented the thought arises concerning oxygen deficiency of tissues as the result of their blockading by the protein elements of the plasma which is coming into the intertissue gaps through the affected capillary walls. In the event of the correctness of a similar assumption in the dynamics of plague infection there should be observed a decrease in the amount of plasma and the clotting of blood. We decided to verify this experimentally. For this purpose we used hematrocrite to determine the amount of plasma in 10 guinea pigs before infection and each day following infection with B. pestis 773 (infecting dose 1,000 microbial bodies). The tests showed that in healthy guinea pigs the amount of plasma was on the average of 71.5%. Under analogous conditions for determining (centrifuging of capillaries with blood for 20 minutes at 5,000 revolutions a minute), after one day following infection the amount of plasma was reduced to 62.2%, that is, almost by 10%. In subsequent days of the infectious process the content of plasma in the blood decreased less intensively (table 6).

The decrease in the content of plasma in the blood creates a foundation for considering that already in the first period of the experimental plague process plasmorrhea takes place and consequently the blockading of its tissue elements by protein components.

Added further to the disruption of vascular permeability is the slowing down of the rate of blood flow, still further aggravating the seriousness of the hypoxia condition of the organism.

The blockading of tissues by the protein masses of perspiring plasma, setting in as a result of an increase of permeability of the vascular wall, sharply changes the course of metabolic processes between the blood and tissues, hinders the sufficient intake of oxygen by the working organs and the removal of the products of cellular metabolism from them. The hypoxia condition which develops as a result of this in its turn furthers the increase of permeability of the capillary endothelium, since it is known that hypoxia alone causes an increase of vascular permeability (N. V. Balanina, 1956).

thus, during plague infection a vicious circle is created -- the infectious onset leads to a disruption of capillary permeability and the [illegible] tissues with their subsequent hypoxia, and the hypoxia still further disrupts the permeability of the vessels and leads to the additional discharge of plasma, and together with this, it must be conjectured, also of bacteria [illegible] from the blood into the tissues, which worsens the hypoxic condition.

Establishment of the fact of plasmorrhea and the decrease in the rate of blood flow during plague infection clear up the data which was obtained earlier. The reason becomes clear for the increase in the amount of hemoglobin in the peripheral blood in plague infected guinea pigs. As a result of the increase in the permeability of the vascular wall and the slowing down of the blood flow, part of the plasma goes out into the intertissue spaces, the clotting of blood takes place, and consequently an increase in the percentage content of hemoglobin in the circulating blood.

It is probable that during plague infection the discharge of plasma from the vascular channel is not the same in all the organs and tissues. The intensity of plasmorrhea depends on the degree of affection of the capillary vessels and the slowing down of capillary blood flow in this or that organ or tissue. In organs with a sharp increase of vascular permeability and a significant slowing down of the blood flow it is natural to expect more intensive plasmorrhea than in those where these changes are not [illegible] since metabolic processes occur, the blood and tissues go [illegible] vessels and the rate of blood flow in these vessels is the highest, then it is natural that plasmorrhea, and consequently the clotting of blood with an increase in the content of hemoglobin are observed in the [illegible] to a greater degree than in blood taken from the heart or [illegible].

The small arteriovenous difference and the presence of relatively [illegible] of oxygen in the venous blood [illegible] become clear. In view of the fact that the blockading of the tissue by protein molecules prevents the delivery of oxygen to the functioning cells, then these cells experience a sharp oxygen deficiency, the oxygen is detained in the capillary and venous blood and is not used at all.

It is probable that the hypoxic condition plays a significant role in the overall chain of functional disruptions which set in in an organism during plague infection. Therefore, any easing of the severity of oxygen deficiency will always favorably influence the course of plague infection.

In the complex method of treating plague patients which was developed by N. N. Zhukov-Verezhnikov, one of the components is methylene blue. By the addition of methylene blue to Sulfidine, N. N. Zhukov-Verezhnikov achieved the transformation of the bacteriostatic effect of Sulfidine in respect to B. pestis to bactericidal. The complex of Sulfidine with methylene blue in conjunction with antiplague serum was a powerful therapeutic means, the use of which for the first time made it possible to cure even the pulmonary form of plague.

It is known that in the processes of biological oxidation methylene blue may play the role of acceptor of hydrogen and by this normalize the course of metabolic processes in the tissues. Therefore, it can be assumed that the influence of methylene blue is not limited just by its bactericidal effect in conjunction with Sulfidine on the plague microbe. The possibility is not excluded of the influences of methylene blue also on the processes of tissue respiration of a macroorganism, which during plague infection is found in a state of hypoxia.

The liquidation of the symptoms of oxygen deficiency doubtlessly would be a significant moment in the general series of symptomatic therapeutic actions on a plague infected organism. However, here it is necessary to take into consideration the whole complex of pathological changes with a decrease in the content of oxygen in the blood, a disruption in the rate of blood circulation, the intensity of absorption, the degree of permeability of capillary membranes, and the discharge of plasma from the vascular channel into the tissues.

Conclusions

1. During experimental plague in guinea pigs a slowing down is observed in the absorption of radioactive phosphorus from the subcellular tissue, progressing with the course of the infectious process.

2. The sharp reduction in the intensity of resorption of the subcutaneously administered radioactive phosphorus testifies to the significant disruptions in the functions of the capillary system during plague in guinea pigs.

3. In the course of plague infection in guinea pigs a decrease is observed in the rate of the blood flow, which in the last days of the infectious process is decreased by almost 2 times in comparison with the initial rate noted prior to infection.

4. During experimental plague infection a disruption is noted in the permeability of the vascular wall and as a result of this the discharge of plasma into the intertissue spaces takes place.

5. The complex of pathological changes with the disruption of the rate of blood flow, intensity of absorption of substances, the degree of permeability of capillary membranes and the discharge of plasma from the vascular channel into the tissues, plays an important role in the overall chain of functional disruptions which set in in the organism of a guinea pig during plague infection.

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Table [illegible]

Rate of resorption of subcutaneously administered $Na_2HP^{32}O_4$ in guinea pig No 8 before infection

Time from onset of recording (in min.)	Number of impulses in 1 min.	Logarithm of number of impulses	Time from onset of recording (in min.)	Number of impulses in 1 min.	Logarithm of number of impulses
1	1280	3.1072	11	676	2.8299
3	1120	3.0492	13	596	2.7752
5	982	2.9921	15	525	2.7202
7	872	2.9405	17	467	2.6693
9	752	2.8762			

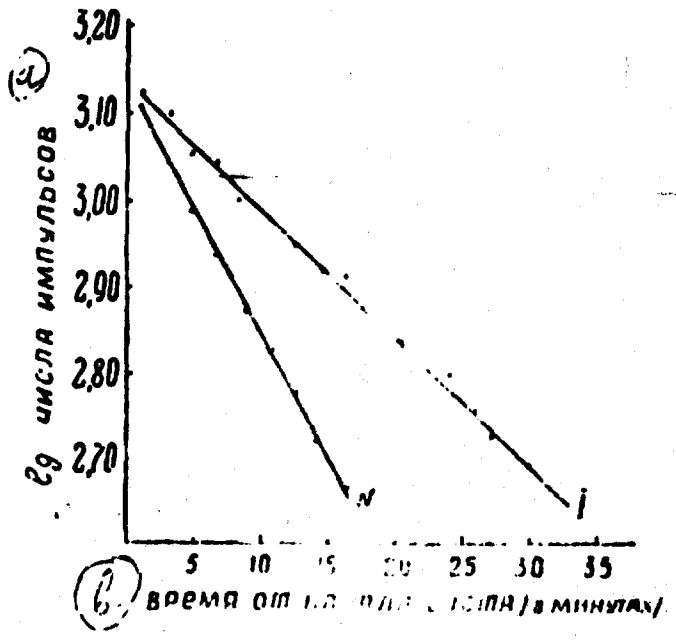

Figure 1. [illegible] resorption of subcutaneously administered $NaHP^{32}O_4$ in guinea pig [illegible] before infection and after 1 day following infection (in the semilogarithmic system of coordinates.
a - lg of the number of impulses; b - time from the onset of calculation (in minutes).

Table 2

Time for the half removal of $Na_2HP^{32}O_4$, determined over the expanse of 4--6 days in healthy guinea pigs

No. of guinea pig	Time for half removal in minutes						Average value
	1st day	2nd day	3rd day	4th day	5th day	6th day	
1	9.5	10	10	10.5	--	10	10
2	14	13	12.5	12.5	11	12	13
3	11	10	10.5	11	10.5	10	10.5
4	12	12.5	13	12.5	12	13	12.5
5	10	11.5	11.5	13.0	11	12	11.5
6	9	9	10	10	--	--	9.5
7	10.5	11.5	10	9.5	10.5	11	10.5
8	11	12	11.5	13	12	12.5	12
9	12	11.5	11	11	12	--	11.5
10	14	15.5	15	13.5	14.5	14.5	14.5
11	12.5	12	12	11.5	11	13	12
12	9	10	10	9.5	9	9.5	9.5
13	12	14	11	12	11.5	--	12
14	16	15	15	14	--	--	15
15	16	18	16	15	15.5	15.5	16
16	14	13.5	13	13.5	--	--	13.5
17	10	9	9	10	9.5	--	9.5
18	14.5	14.5	16	14	15	13	14.5
19	12	10	13	9	10	9	10.5
20	15	14	14	13	14	--	14

Table 3

Rate of resorption of subcutaneously administered $Na_2HP^{32}O_4$ in guinea pig No 8 after 1 day following infection with plague

Time from onset of recording (in min.)	Number of impulses in 1 min.	Logarithm of number of impulses	Time from onset of recording (in min.)	Number of impulses in 1 min.	Logarithm of number of impulses
1	1352	3.1303	19	771	2.8871
3	1260	3.1004	21	682	2.8338
5	1162	3.0645	23	664	2.8222
7	1134	3.0531	25	640	2.8062
9	1014	3.0043	27	572	2.7574
11	944	2.9750	29	532	2.7259
13	866	2.9523	31	500	2.6990
15	842	2.9253	33	472	2.6739
17	815	2.9112	35	460	2.6622

Table 4

Time for the half removal of subcutaneously administered $Na_2HP^{32}O_4$ in the dynamics of plague infection (in minutes)

No. of guinea pig	Before infection	After infection (in days)						After how many days following infection animal was destroyed or died
		1	2	3	4	5	6	
1	10	21	--	--	--	--	--	1 (d)
2	13	20	27	-	--	--	--	2 (d)
3	10.5	29.5	55	1	--	--	--	3 (d)
4	12.5	18	25	29	--	--	--	3 (d)
5	11.5	19	31	36	43	--	--	1 (d)
6	9.5	18.5	43	54	--	--	--	3
7	10.5	19	23	32	52	--	--	4 (d)
8	12	21.5	29	37	49	[illegible]	--	5
9	11.5	22.5	27	43	59	--	--	4
10	14.5	19	31	38	--	--	--	3
11	12	16.5	1[illegible]	29	32	38	--	5
12	9.5	14.5	24	[illegible]	[illegible]	65	--	5
13	12	23	3[illegible]	[illegible]	[illegible]	--	--	4
14	15	16	31	50	62	--	--	1
15	16	23	28	38	54	70	--	5
16	13.5	20.5	25	34	49	61	--	5 (d)
17	9.5	19	31	36	[illegible]	--	--	1
18	14.5	16	29	40	51	70	80	6 (d)
19	10.5	27	37	5[illegible]	--	--	--	3
20	14	21	[illegible]	43	67	8[illegible]	--	5
M	12.1	20.3	2[illegible].1	41	10.1	[illegible].7	[illegible].0	

Legend: M - average arithmetic [illegible]
d - destroyed

Table 5

Rate of blood flow in healthy guinea pigs and following their infection with B. pestis (average values)

Before infection	After infection			
	1 day	2 days	4 days	5 days
5.1 sec	6.5 sec	7.2 sec.	9.6 sec	9.8 sec

Table 6

Percentage content of plasma in the blood of guinea pigs in the dynamics of plague infection

No. of pig	Before infec.	After infection				
		1 day	2 days	3 days	4 days	5 days
1	72	66	64	65	63	58
2	73	56	60	58	59	--
3	68	67	57	55	57	53
4	70	67	67	66	65	64
5	70	62	65	63	64	65
6	65	58	55	56	53	--
7	71	57	56	57	--	--
8	73	66	66	64	62	60
9	70	58	56	57	--	--
10	74	67	63	65	62	--
Average	71.5	62.2	61	60.6	60.6	60